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Réticulé absorbent copolymer of medical use and ancillary medical.

The present invention relates to a product with medical and ancillary medical use, given that that these terms must be taken in their acceptances more broad. By < use; RTI ID=1.1> medical?, < /RTI> one will also hear ?use veterinary surgeon " and ?surgical use?, while by ?ancillary medical use?, one will understand also the ?uses of care ", the ?dietetic uses?, as well as the uses titrates ration of survival?.

The product defined above is primarily made up of an absorbent copolymer of the acrylamide type/réticulé alkaline acrylate or vinyl alcohol/réticulé alkaline acrylate and the invention will be described hereafter in reference more particularly and respectively to copolymers of the acrylamide and < RTI ID=1.2> the acrylate< /RTI> of sodium, and vinyl alcohol and of < RTI ID=1.3> the acrylate< /RTI> of sodium, which constitutes the preferred products.

The copolymers of the acrylamide and the réticulés sodium acrylate are well-known for their employment in fields as various as in agriculture and in the industry of the adhesives and the powders used in reproduction colors. < RTI ID=1.4> I< /RTI> is necessary to say that they have the property to gel in aqueous mediums and to absorb, according to the granulometry of the powders in the form of which they are presented, several hundreds of times their own volume of water.

All great names of medical chemistry and others are associated this kind of copolymers, for example Hoechst, Minnesota Mining, Of the Bridge De Nemours, Eastman Kodak, Hitachi, Suminomo Chemical, Fuji Photo, Ricoh, Toray Industries, Yasuda

The present invention aims at uses of such a product in an extremely different technical field, since they are the medical and ancillary medical fields in the broad sense indicated above. One < RTI ID=2.1> srest< /RTI> outline indeed that the copolymers had, with respect to the human organism and animal, of the properties of ?neutrality? which allowed them this kind of applications.

The invention thus relates to a product of medical and ancillary medical use, characterized in that it is primarily made up of a réticulé alkaline absorbent copolymer, following elementary reasons

EMI2.1

where R1, R2, < RTI ID=2.2> R3< /RTI> < RTI ID=2.3> R1 R2< /RTI> R3 which can be identical or different are hydrogen atoms or groups alkyls < RTI ID=2.4> C1 - C3, < /RTI> Represent me an alkaline metal and Z represents OH or group CONH2.

Products preferred among the range indicated above are those where R1 = R2 = R3 = R1 < RTI ID=2.5> = < /RTI> R2 = R3 = H, Me = Na and Z = CONH2 < RTI ID=2.6> ciest-with-dire< /RTI> copolymers of < RTI ID=2.7> the acrylamide< /RTI> and of the sodium acrylate themselves as follows

EMI3.1

< RTI ID=3.1> or where R1 = R2 = R3 = R1 = R2 R2 Me 3< /RTI> and Z = OH, i.e. copolymers of vinyl alcohol and the sodium acrylate themselves, as follows

EMI3.2

This product can be powder tiny room, advantageously having an average diameter of particle ranging between 50 and 700 < RTI ID=3.2> u< /RTI> m, preferably around < RTI ID=3.3> 250< /RTI> m, at the dry state. In this form, it gels into present of any aqueous medium (water, serum, etc) or hydroalcoholic while absorbing between 500 and 700 times its volume of water. The process of gelation is relatively fast, since it is necessary between 0.5 and 5 mn to acquire maximum and final swelling in aqueous medium.

Soaked, the powder has an average diameter of particles ranging between 450 and 6200 < RTI ID=3.4> p< /RTI> m, preferably around 3000 < RTI ID=3.5> P< /RTI> Mr.

This powder has a total harmlessness visà-screw of the higher beings, in particular of the mammals and < RTI ID=3.6> the homme< /RTI> One measured a lethal amount 50 indeed at the mouse and the rat higher than 10 kg/kg body: One could not highlight any effect of irritation on skin intact and abraded in rabbit, after 24h, nor at the man; no irritation of the eye in rabbit; no irritation of the vaginal membrane at

bitch; no the haemolytic effect on the érythrocytes in rabbit, the dog and the man and not of effect < RTI ID=4.1> antigénique< /RTI> in the dog. Other tests will be described in the examples.

The products thus authorize the various uses mentioned above.

A first use which will be described thereafter more in details, is likely to interest the dieticians, < RTI ID=4.2> puisqu'il< /RTI> aim at fighting the bulimia and obesity, for example by means of reducing diets.

Indeed, the product according to the invention, preferably conditioned in the form of gélules, can be absorbed by oral way and will inflate in the stomach by filling this one and cutting the feeling of hunger. As it later on will be seen and as that will be described in details in the examples, the product according to the invention is not absorbed by the organization and is thus completely neutral with respect to this one. Once its function filled, which is to cut the hunger by saturating the stomach, it progresses just as it is and without any transformation in the intestine to be to evacuate by the natural ways. One will be able to note in certain cases a very light laxative effect, which is rather an element favorable for the type of use quoted above.

It can consequently be built-in in a mode slimming, where it replaces most of food by decreasing in a corresponding way the contribution of those on the heating level or of the nutrients.

In such uses, the product according to the invention is introduced just as it is, without other excipients that those necessary to the form of conditioning or the galenic form considered.

Another use consists in fixing on the product according to the invention, in calculated quantity, the nutrients (proteins, lipids, glucids, vitamins, rock salt, trace elements, etc?) necessary to the human organism, in order to constitute rations of survival more appetizing than a concentrate or pills, while having the advantage, like above, to cut the feeling of hunger dictated by the stomach.

Another important field of use of the product according to the invention is that of the care. Thus, in the field of the care of hygiene or simply of comfort, the product according to the invention can be conditioned, in a form adapted, in an envelope in woven or not woven according to the type of application and to be used for its properties of absorption like bandages and < RTI ID=5.1> Sompreses, < /RTI> by making profitable its very great faculties < RTI ID=5.2> i' absorption< /RTI> liquids. In the same way, one can constitute of them draw sheets, or layers for babies or < RTI ID=5.3> dultes< /RTI> incontinent. It can be also conditioned, in an adapted form, like towels or tampons where its absorbing properties will be very < RTI ID=5.4> ippréciées.< /RTI>

In the field of the medical care, impregnated or not of an active ingredient having healing virtues or healing and placed, in an adapted envelope, it can be used like compresses surgical or < RTI ID=6.1> dry plaster or humide.< /RTI>

In the properly medical, interesting field thus allopaths as long as homeopaths, the product according to the invention < RTI ID=6.2> hêtre< can: /RTI> impregnated of an active ingredient and being deposited on the surface of the organization or being conveyed inside this one. Introduced by oral way, it can be used as gastric bandage to protect the intestinal mucous membrane and to treat, to calm the pain in the gastro-intestinal gastrites, oesophagites, ulcers, the colites, the polyposes, polyps, etc

In this same medical field, the product according to the invention impregnated of an active ingredient can be used for an internal topics application, the copolymers protecting the active ingredient from degradation too fast and thus making it possible to forward this one on the site where it must act.

By external way, the product according to the invention impregnated of an active ingredient can be applied locally, either by way of injection, or directly to the skin or this last will act with the manner of transdermique.

One can also consider the use in oncology, by internal or external way, the product according to the invention being in charge of an active ingredient (chemotherapy) or with one radioelement (radiotherapy).

Another important use, where the product is use in the presence of liquid, at the beginning of its gelation, comes within province of the surgery, in particular plastic surgery. Indeed, after gelation, the product according to the invention constitutes excellent substance of maintenance or filling, inert opposite organization and in practice nonbiodegradable. One will use then by injection or incision for treatment of the wrinkles for example, the ptoses mammaires or like prosthesis or plastie, testicles, etc

The invention will be included/understood better in reference with the examples, given hereafter on a purely nonrestrictive basis. These examples show the harmlessness of the product according to the invention and, consequently, its great faculty of employment in the fields mentioned above, in particular, in dietetics and in the field of the care.

Example 1

Elimination by digestive tract

Because of the size of the inflated water particles, there is little chance so that those can cross the barrier of the intestinal wall.

To check it, five patients received during three days a daily amount of 10,0 G copolymer OIGETAGEL < RTI ID= 7.1> prégonf lé< /RTI> in two catches, in 250 ml of mineral water. This copolymer is available near company OMAREX in Schlieren ZH, Switzerland.

As of the first day, the saddles were collected during five days. They were washed and filtered through a filter of porosity of 500 Mr.

The matter collected was joined together and weighed in end of the period of observation. The recovered weight is following it for the five subjects:

1. < RTI ID=8.1> 24.6< /RTI> G 2. 26.3 G 3. 28.2 G - 4. 25.1 G 5. 27.2 G

The average value of recovery is 26,88 G what, taking into account the losses due to handling, represents a quasi total elimination of the product.

Moreover, with the microscopic examination of the particles, the form and the structure do not appear different from what they are at the beginning. The digestive course of the particles does not modify their nature and structure.

Example 2

Study of the susceptibility of copolymer to the enzymes

Samples of particles of copolymer were put in the presence of water to obtain a maximum swelling. Freezing was dispersed with a Vortex and a suspension of 50.000 particules/ml was prepared. A sample of this front suspension put in the presence of the following enzymes

- Amylase 10, 50, 100 meg/ml
- Trypsin 10, 50, 100 meg/ml
- Pepsin 10, 50, 100 meg/ml

The front suspensions were incubated during four hours in an incubator at 37° C. After incubation, them cells were counted. The number of cells recovered of the m even order of magnitude is that the whole initial sample (- between 49250 and 50015). By elsewhere, the weight after centrifugation is the same one as that observed at the beginning of the experiment.

Copolymer particles, inflated water do not seem to be attacked by the enzymes used.

This result confirms the results concerning elimination by digestive tract.

Example 3

Study of < RTI ID=9.1> AI; /RTI>

The goal of this study is to determine the allergenic potentiality of the copolymer particles.

With this intention, an amount of twice 2,0 g/jour, in water présenec, is managed during 5 days on 20 voluntary subjects.

Before the beginning of the test and four days after the end of this last, the test following were practised

1. A prick-test with the substance inflated, reading of the cutaneous answer after twenty minutes and two hours (immediate over-sensitiveness).

2. A patch-test with the substance inflated with reading after 24 and 48 hours (over-sensitiveness with cellular mediation).

At all the subjects, the immediate tests as well as late are remained negative. The copolymer thus seems inert on the immunological level.

3 subjects out of the 20 introduced into the study complained about a certain gastric heaviness during one to two hours after the catch of copolymer. There was however no complaint of gastric or enterocolic pain. Lastly, a light laxative effect was raised by all the subjects.

It should be noted that such effects, if they checked in a systematic way on a great number of subjects, are not negative, quite to the contrary, within the framework of a dietetic application of slimming. The physiological feeling of hunger is gummed and the intestinal transit time is facilitated.

Example 4

Study of the cellular behavior in vitro

One analyzes the behavior of the cells immunocompétentes and phagocytic with respect to the copolymer particles. In the measurement or certain particles of low size could possibly cross intestinal wall, it is useful of connaltre their to become

and their effects on the functions immunes.

a) Test of cytotoxicity

Increasing concentrations of particles

inflated (of 20.000 - 200.000) were put in presence

of a constant population < RTI ID=11.1> te< /RTI> lymphomonocytes coming

allergic patients. Incubation was practised in

medium RPMI in the presence of 10% of human serum < RTI ID=11.2> AB, < /RTI> It

was four hours. The cells were then put

in the presence of blue of Trypan and in the 10 minutes of

the setting in contact, the number of viable cells was

determine.

The results are as follows, in value

average of ten samples

% of viable cells

Control 93%

S. 20.000 95 < RTI ID=11.3> %< /RTI>

S. 100.000 88%

S. 200.000 92 < RTI ID=11.4> %< /RTI> b) Test of lymphocytary stimulation

Ten cultures of lymphomonocytes were practised, the cells coming from allergic subjects.

A five days incubation was practised in a medium RPMI plus 15% of serum AB.

The cultures consisted of < RTI ID=12.1>

- 1 batch of control (phytohemagglutinine) stim. lymph. T

- 1 batch with PHA mitogene (lectines, mègeine végétale)

- 1 batch with Idiot-A (concavaline A) stim. lymph. B

Three parallel batches were cultivated with however in

more 50.000 copolymer gonflées/ml particles of

medium. After incorporation of 3H-Thymidine (1,0 uc/106

cells) the cells are washed and the activity

isotopic estimated in a scintillation counter

liquid (Beckmann). The results are expressed in one

blow per minute (cpm). < /RTI>

The results obtained are as follows

Cpm + SE < RTI ID=12.2>

1. Control 369 ± 17

2. Control + particles 375 ± 21< /RTI>

2a. PHA 76.593 ± 7 250

2a. PHA < RTI ID=12.3> +< /RTI> particles. 74.781 ± 5 720

3. Idiot-A 28.513 ± 1 780

3a. Idiot-A < RTI ID=12.4> t< /RTI> particles 29.557 ± 2.046 < RTI ID=12.5>

The statistical analysis (+ - test of student) does not show any statistically significant difference enters, respectively 1

and; 2 and 2a; 3 and 3a.

In conclusion, with the concentration used, the copolymer particles do not interfere with the proliferation

lymphomonocyte in vitro. < /RTI>

c) Test of phagocytosis

The polynuclear ones coming from patients

allergic insulated on gradients from Ficoll-Isopaque- have

summer washed and en milieu RPMI put in the presence of particles

of copolymer. The cell ratio/particle < RTI ID=13.1> was of 1/5.< /RTI>

Fifteen experiments were practised. The suspension

cellular was incubated during two hours at 37° C.

separation of the couple cell/particles was made by

sedimentation in hypotonic aqueous medium.

In each test, five hundred cells

polynuclear were counted and the presence of

intracellular particles given.

It was not observed of phagocytose of

particles Indeed, the inflated particles are

so much larger than the cells than

phagocytosis is hardly possible. On the other hand, of

the shapes of rivet washer were noted, < RTI ID=13.2> ttest-with-dir< /RTI> four

eight polynuclear coupled with the periphery of a particle probably in an attempt at phagocytose.

An identical test was developed this foisci by using monocytes insulated on plate from glass.

Here also, it was not observed of phagocytose, but some rivet washers of the < RTI ID=13.3> mène< /RTI> type that

those observed with the polynuclear ones.

Phagocytic, polynuclear cells I.E.(internal excitation)

monocytes is not capable of phagocyt < RTI ID=14.1> lecc< /RTI>

particles of vinyl/acrylic.

Example 5

Compress

< RTI ID=14.2> prépare< /RTI> compress of 40 X 40 cm for

4 mm thickness by locking up balls of copolymer of mark < RTI ID=14.3> # IGETAGEL< /RTI> sold by OMAREX in an envelope of not woven, which, in alternative, can be in its covered turn < RTI ID=14.4> of une< /RTI> traditional gauze.

These compress are applied to wounds where their absorbing properties make wonder compared to compress traditional. Moreover, they constitute a remarkable barrier < RTI ID=14.5> contre< /RTI> the infection of the wounds by germs come from outside.